



SEQUENCE LISTING

<110> BLACK, Roy A.
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NASKOS, Klaus
FERNANDEZ-CATALAN, Carlos
CHEN, James Ming
LEVIN, Jeremy Ian

<120> Crystalline TNF-alpha-converting enzyme
and uses thereof

<130> 16163-039004

<140> US 10/784,300
<141> 2004-02-24

<150> US 09/244,984
<151> 1999-02-04

<150> US 60/073,709
<151> 1998-02-04

<150> US 60/135,499
<151> 1998-03-30

<150> US 60/117,476
<151> 1999-01-27

<160> 10

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Illustrative peptide

<400> 1
Pro Leu Ala Gln Ala Val Arg Ser Ser Ser
1 5 10

<210> 2
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Illustrative peptide

<400> 2

Gly Ser His His His His His His

1

5

<210> 3

<211> 11

<212> PRT

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<220>

<223> Consensus motif

<220>

<221> VARIANT

<222> 3, 4, 6, 7, 9, 10

<223> Xaa = any amino acid

<400> 3

His Glu Xaa Xaa His Xaa Xaa Gly Xaa Xaa His

1

5

10

<210> 4

<211> 203

<212> PRT

<213> Crotalus adamanteus

<400> 4

Glu Gln Asn Leu Pro Gln Arg Tyr Ile Glu Leu Val Val Val Ala Asp

1

5

10

15

Arg Arg Val Phe Met Lys Tyr Asn Ser Asp Leu Asn Ile Ile Arg Thr

20

25

30

Arg Val His Glu Ile Val Asn Ile Ile Asn Glu Phe Tyr Arg Ser Leu

35

40

45

Asn Ile Arg Val Ser Leu Thr Asp Leu Glu Ile Trp Ser Gly Gln Asp

50

55

60

Phe Ile Thr Ile Gln Ser Ser Ser Ser Asn Thr Leu Asn Ser Phe Gly

65

70

75

80

Glu Trp Arg Glu Arg Val Leu Leu Thr Arg Lys Arg His Asp Asn Ala

85

90

95

Gln Leu Leu Thr Ala Ile Asn Phe Glu Gly Lys Ile Ile Gly Lys Ala

100

105

110

Tyr Thr Ser Ser Met Cys Asn Pro Arg Ser Ser Val Gly Ile Val Lys

115

120

125

Asp His Ser Pro Ile Asn Leu Leu Val Ala Val Thr Met Ala His Glu

130

135

140

Leu Gly His Asn Leu Gly Met Glu His Asp Gly Lys Asp Cys Leu Arg

145

150

155

160

Gly Ala Ser Leu Cys Ile Met Arg Pro Gly Leu Thr Pro Gly Arg Ser

165

170

175

Tyr Glu Phe Ser Asp Asp Ser Met Gly Tyr Tyr Gln Lys Phe Leu Asn

180

185

190

Gln Tyr Lys Pro Gln Cys Ile Leu Asn Lys Pro

195

200

<210> 5
 <211> 287
 <212> PRT
 <213> Homo sapiens

<400> 5
 Pro Glu Glu Leu Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro
 1 5 10 15
 Met Lys Asn Thr Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr
 20 25 30
 Arg Tyr Met Gly Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile
 35 40 45
 Glu Leu Ile Asp Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp
 50 55 60
 Asn Ala Gly Phe Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile
 65 70 75 80
 Leu Lys Ser Pro Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met
 85 90 95
 Ala Lys Ser Tyr Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met
 100 105 110
 Leu Leu Glu Gln Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val
 115 120 125
 Cys Leu Ala His Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu
 130 135 140
 Gly Leu Ala Tyr Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val
 145 150 155 160
 Cys Pro Lys Ser Gly Ser Ser Gly Gly Ile Cys Glu Lys Ala Tyr Tyr
 165 170 175
 Ser Pro Val Gly Lys Lys Asn Ser Lys Leu Tyr Ser Asp Gly Lys Lys
 180 185 190
 Lys Glu Ala Asp Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly
 195 200 205
 Ala Glu His Asp Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp
 210 215 220
 Gln Gly Gly Lys Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His
 225 230 235 240
 Glu Asn Asn Lys Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys
 245 250 255
 Thr Ile Glu Ser Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys
 260 265 270
 Val Cys Gly Asn Ser Arg Val Asp Glu Gly Glu Glu Cys Asp Pro
 275 280 285

<210> 6
 <211> 276
 <212> PRT
 <213> Homo sapiens

<400> 6
 Gln Glu Lys His Ala Ile Asn Gly Pro Glu Leu Leu Arg Lys Arg Arg
 1 5 10 15
 Thr Thr Ser Ala Glu Lys Asn Thr Cys Gln Leu Tyr Ile Gln Thr Asp
 20 25 30
 His Leu Phe Phe Lys Tyr Tyr Gly Thr Arg Glu Ala Val Ile Ala Gln
 35 40 45
 Ile Ser Ser His Val Lys Ala Ile Asp Thr Ile Tyr Gln Thr Thr Asp

50		55		60
Phe Ser Gly Ile Arg Asn Ile Ser Phe Met Val Lys Arg Ile Arg Ile				
65		70		80
Asn Thr Thr Ala Asp Glu Lys Asp Pro Thr Asn Pro Phe Arg Phe Pro				
	85		90	95
Asn Ile Ser Val Glu Lys Phe Leu Glu Leu Asn Ser Glu Gln Asn His				
	100		105	110
Asp Asp Tyr Cys Leu Ala Tyr Val Phe Thr Asp Arg Asp Phe Asp Asp				
	115		120	125
Gly Val Leu Gly Leu Ala Trp Val Gly Ala Pro Ile Tyr Leu Asn Ser				
	130		135	140
Gly Leu Thr Ser Thr Ser Leu Asn Thr Gly Ile Ile Thr Val Lys Asn				
	145		150	155
Tyr Gly Lys Thr Ile Leu Thr Lys Gln Asn Tyr Gly Ser His Val Pro				
	165		170	175
Pro Lys Val Ser His Ile Thr Phe Ala His Glu Val Gly His Asn Phe				
	180		185	190
Gly Ser Pro His Asp Ser Gly Thr Glu Cys Thr Pro Gly Glu Ser Lys				
	195		200	205
Asn Leu Gly Gln Lys Glu Asn Gly Asn Tyr Ile Met Tyr Ala Arg Ala				
	210		215	220
Thr Ser Gly Asp Lys Leu Asn Asn Asn Lys Phe Ser Leu Cys Ser Ile				
	225		230	235
Arg Asn Ile Ser Gln Val Leu Glu Lys Lys Arg Asn Asn Cys Phe Val				
	245		250	255
Glu Ser Gly Gln Pro Ile Cys Gly Asn Gly Met Val Glu Gln Gly Glu				
	260		265	270
Glu Cys Asp Cys				
	275			

<210> 7
 <211> 824
 <212> PRT
 <213> Homo sapiens

<400> 7
Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu
1 5 10 15
Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu
20 25 30
Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser
35 40 45
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr
50 55 60
His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys
65 70 75 80
Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val
85 90 95
Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Ala Lys Trp Gln
100 105 110
Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu
115 120 125
Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly
130 135 140
Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys
145 150 155 160

Asp	Lys	Arg	Met	Leu	Val	Tyr	Lys	Ser	Glu	Asp	Ile	Lys	Asn	Val	Ser	165	170	175
Arg	Leu	Gln	Ser	Pro	Lys	Val	Cys	Gly	Tyr	Leu	Lys	Val	Asp	Asn	Glu	180	185	190
Glu	Leu	Leu	Pro	Lys	Gly	Leu	Val	Asp	Arg	Glu	Pro	Pro	Glu	Glu	Leu	195	200	205
Val	His	Arg	Val	Lys	Arg	Arg	Ala	Asp	Pro	Asp	Pro	Met	Lys	Asn	Thr	210	215	220
Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr	Arg	Tyr	Met	Gly	225	230	235
Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile	Glu	Leu	Ile	Asp	245	250	255
Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp	Asn	Ala	Gly	Phe	260	265	270
Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile	Leu	Lys	Ser	Pro	275	280	285
Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met	Ala	Lys	Ser	Tyr	290	295	300
Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met	Leu	Leu	Glu	Gln	305	310	315
Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val	Cys	Leu	Ala	His	325	330	335
Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu	Gly	Leu	Ala	Tyr	340	345	350
Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val	Cys	Pro	Lys	Ala	355	360	365
Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile	Tyr	Leu	Asn	Ser	Gly	Leu	370	375	380
Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Glu	Ala	Asp	385	390	395
Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly	Ala	Glu	His	Asp	405	410	415
Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp	Gln	Gly	Gly	Lys	420	425	430
Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His	Glu	Asn	Asn	Lys	435	440	445
Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys	Thr	Ile	Glu	Ser	450	455	460
Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys	Val	Cys	Gly	Asn	465	470	475
Ser	Arg	Val	Asp	Glu	Gly	Glu	Glu	Cys	Asp	Pro	Gly	Ile	Met	Tyr	Leu	485	490	495
Asn	Asn	Asp	Thr	Cys	Cys	Asn	Ser	Asp	Cys	Thr	Leu	Lys	Glu	Gly	Val	500	505	510
Gln	Cys	Ser	Asp	Arg	Asn	Ser	Pro	Cys	Cys	Lys	Asn	Cys	Gln	Phe	Glu	515	520	525
Thr	Ala	Gln	Lys	Lys	Cys	Gln	Glu	Ala	Ile	Asn	Ala	Thr	Cys	Lys	Gly	530	535	540
Val	Ser	Tyr	Cys	Thr	Gly	Asn	Ser	Ser	Glu	Cys	Pro	Pro	Pro	Gly	Asn	545	550	555
Ala	Glu	Asn	Asp	Thr	Val	Cys	Leu	Asp	Leu	Gly	Lys	Cys	Lys	Asp	Gly	565	570	575
Lys	Cys	Ile	Pro	Phe	Cys	Glu	Arg	Glu	Gln	Gln	Leu	Glu	Ser	Cys	Ala	580	585	590
Cys	Asn	Glu	Thr	Asp	Asn	Ser	Cys	Lys	Val	Cys	Cys	Arg	Asp	Leu	Ser	595	600	605
Gly	Arg	Cys	Val	Pro	Tyr	Val	Asp	Ala	Glu	Gln	Lys	Asn	Leu	Phe	Leu			

610		615		620
Arg Lys Gly Lys Pro Cys Thr Val Gly Phe Cys Asp Met Asn Gly Lys				
625		630		640
Cys Glu Lys Arg Val Gln Asp Val Ile Glu Arg Phe Trp Asp Phe Ile				
	645		650	655
Asp Gln Leu Ser Ile Asn Thr Phe Gly Lys Phe Leu Ala Asp Asn Ile				
	660		665	670
Val Gly Ser Val Leu Val Phe Ser Leu Ile Phe Trp Ile Pro Phe Ser				
	675		680	685
Ile Leu Val His Cys Val Asp Lys Lys Leu Asp Lys Gln Tyr Glu Ser				
	690		695	700
Leu Ser Leu Phe His Pro Ser Asn Val Glu Met Leu Ser Ser Met Asp				
705		710		720
Ser Ala Ser Val Arg Ile Ile Lys Pro Phe Pro Ala Pro Gln Thr Pro				
	725		730	735
Gly Arg Leu Gln Pro Ala Pro Val Ile Pro Ser Ala Pro Ala Ala Pro				
	740		745	750
Lys Leu Asp His Gln Arg Met Asp Thr Ile Gln Glu Asp Pro Ser Thr				
	755		760	765
Asp Ser His Met Asp Glu Asp Gly Phe Glu Lys Asp Pro Phe Pro Asn				
	770		775	780
Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val				
785		790		800
Ala Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg				
	805		810	815
Val Asn Ser Lys Glu Thr Glu Cys				
	820			

<210> 8

<211> 477

<212> PRT

<213> Homo sapiens

<400> 8

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu				
1		5		10
Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu				
	20		25	30
Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser				
	35		40	45
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr				
	50		55	60
His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys				
65		70		75
Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val				
	85		90	95
Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln				
	100		105	110
Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu				
	115		120	125
Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly				
	130		135	140
Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys				
145		150		155
Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser				
	165		170	175

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Arg Leu Gln Ser Pro Lys Val Cys Gly Tyr Leu Lys Val Asp Asn Glu
      180      185      190
Glu Leu Leu Pro Lys Gly Leu Val Asp Arg Glu Pro Pro Glu Glu Leu
      195      200      205
Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro Met Lys Asn Thr
      210      215      220
Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr Arg Tyr Met Gly
225      230      235      240
Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile Glu Leu Ile Asp
      245      250      255
Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp Asn Ala Gly Phe
      260      265      270
Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile Leu Lys Ser Pro
      275      280      285
Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met Ala Lys Ser Tyr
      290      295      300
Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met Leu Leu Glu Gln
305      310      315      320
Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val Cys Leu Ala His
      325      330      335
Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu Gly Leu Ala Tyr
      340      345      350
Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val Cys Pro Lys Ala
      355      360      365
Tyr Tyr Ser Pro Val Gly Lys Lys Asn Ile Tyr Leu Asn Ser Gly Leu
      370      375      380
Thr Ser Thr Lys Asn Tyr Gly Lys Thr Ile Leu Thr Lys Glu Ala Asp
385      390      395      400
Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly Ala Glu His Asp
      405      410      415
Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp Gln Gly Gly Lys
      420      425      430
Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His Glu Asn Asn Lys
      435      440      445
Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys Thr Ile Glu Ser
      450      455      460
Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys Val
465      470      475

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<210> 9

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetically generated peptide

<400> 9

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Ser Pro Leu Ala Gln Ala Val Arg Ser Ser Ser Arg
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<210> 10

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Illustrative Met-turn located in SEQ ID NOS 5 and
6

<400> 10

Tyr Val Met Tyr

1